TRANSLATION

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
PCT 7504		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/DE2004/002503	12.11.2004	14.11.2003
International Patent Classification (IPC) or national classification and IPC		
C07K16/44 A61K39/00		
Applicant		
VOLLMERS, Heinz		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 12 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *(sent to the applicant and to the International Bureau)* a total of 5 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))

      _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☒	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

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International application No.
PCT/DE2004/002503

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (Rule 12.3 and 23.1(b))

☐ publication of the international application (Rule 12.4)

☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:

pages 1-24 as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ the claims:

nos. _____ as originally filed/furnished

nos.* _____ as amended (together with any statement) under Article 19

nos.* 1-24 received by this Authority on 17.02.2006 with telefax

nos.* _____ received by this Authority on _____

☒ the drawings:

sheets 1-11 as originally filed/furnished

sheets* _____ received by this Authority on _____

sheets* _____ received by this Authority on _____

☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☒ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☒ the claims, nos. 25,26

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

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Box No. II Priority

1. ☒ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:

   ☒ copy of the earlier application whose priority has been claimed (Rule 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 66.7(b)).

2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rule 64.1). Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 4,5,19-24 all in part

because:

☐ the said international application, or the said claims Nos. _____
relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 4,5,19-24

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
☐ has not been furnished
☐ does not comply with the standard

the computer readable form
☐ has not been furnished
☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

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Box No. IV Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees the applicant has:

   ☐ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ neither restricted the claims nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:

   ☒ complied with.

   ☐ not complied with for the following reasons:

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1–3, 6–18 all in full, 4, 5, 19–24 all in part

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Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-16, 18-24	YES
	Claims	17	NO
Inventive step (IS)	Claims	1-16, 18-24	YES
	Claims	17	NO
Industrial applicability (IA)	Claims	1-24	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Reference is made to the following documents:

D1: GETZ G S: "The first human monoclonal antibody to oxidized LDL." ARTERIOSCLEROSIS, THROMBOSIS, AND VASCULAR BIOLOGY. AUG 2001, Vol. 21, No. 8, August 2001 (2001-08), pages 1254-1255, XP002333218 ISSN: 1524-4636

D2: WO 03/048321 A (ALEXION PHARMACEUTICALS) 12 June 2003 (2003-06-12).

1. Novelty of claim 17

Figure 3a of document D2 discloses sequences of VL chains of antibodies. CDR3-7, for example, comprises CDR1 and CDR2 regions, which are identical to those specified in claim 17. Document D2 is therefore prejudicial to the novelty of claim 17, and to that of claims 18 and 19, which refer back to claim 17.

2. Inventive step of claims 1 and 20-24

Document D1 describes a human monoclonal antibody

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

which binds specific oxidized LDL. Document D1 also discusses the therapeutic use of this antibody in the diagnosis of atherosclerosis. However, contrary to document D1, the antibody SAM-6.10 causes more oxidized LDL particles to be absorbed by macrophages. This results in a specific lowering of blood LDL levels, thereby reducing a significant risk factor for heart and vascular disease. In the light of the teaching of document D1 this is a surprising effect. Consequently, independent claim 1 is in principle inventive, as are claims 20-24, directed to medical uses. See, however, the observations made in Box VIII.

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claim 1 comprises alternatives in the form of polypeptides which consist of the VI (SEQ ID No:1) or the Vh domain (SEQ ID No:3). However, it would appear questionable whether the VI or the Vh domain alone continue to have the antigen binding properties which the applicant has demonstrated only for the intact, full antibody SAM-6.10. Claims 1-11, 14-17 and 20-26 are therefore not disclosed in the application (PCT Article 5). The same applies to claims 14-16, which do not contain the functional feature of (ox)LDL binding.

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing

   ☒ contained in the international application as filed

   ☒ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment* on _____

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

* *If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."*

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**
Continuation of: Box III and IV.4

Box III

Lack of unity of invention

Owing to lack of unity of invention the claims of the group of inventions 2 (claims 4, 5, 19, 20-24, all in part) are not the subject of the international search report (see also Box IV).

Box IV.4

The different inventions/groups of inventions are:

Invention 1: claims 1-3, 6-11, 14-17, all in full;
claims 4, 5, 19-24, all in part:

a purified polypeptide which is identical to the amino acid sequences of SEQ ID No:1 and/or SEQ ID No:2, and binds the low density lipoprotein (LDL) and/or oxidized LDL (oxLDL).

Invention 2: claims 4, 5, 19, 20-24, all in part:

An antibody of a functional fragment thereof.

For the following reasons these inventions/groups of inventions are not so linked as to form a single general inventive concept (PCT Rule 13.1):

Supplemental Box

In order for several groups of inventions in an application to satisfy the unity of invention requirement of PCT Rule 13.1, they must be linked by a shared or corresponding special technical feature. This means that the common technical feature must make a contribution to the teaching of the prior art, that is to say, it has to be novel and inventive. In the present case claim 1 is restricted to a polypeptide which is identical to the amino acid sequences of SEQ ID No:1 and/or SEQ ID No:2. These SEQ ID Nos. represent the VI and Vh chain of the monoclonal human antibody SAM-6.10. The claimed polypeptide is therefore either the Vh or the VI domain or a fragment of the Fab fragment of SAM-6.10, this Fab fragment consisting of the two N-terminal variable domains of SAM-6.10. In addition, the polypeptide of claim 1 is characterized by a functional feature, that is to say the binding to (oxidized) LDL.

Claim 4 concerns a polypeptide which is an antibody or a functional fragment thereof. The nature of the functional fragment is not restricted. This is further clarified by dependent claim 5, which is limited to polypeptides which are, for example, Fc fragments. However, an Fc fragment does not contain the N-terminal variable domains of the light and the heavy chain. The common technical feature of claims 4 and 5, insofar as they do not relate to the VI and Vh domains of claim 1, and of claim 1, is therefore "fragment of an antibody". This common technical feature is, *a priori*, likewise, not a special technical feature.

Consequently, claims 19-24 also do not meet the unity of

Supplemental Box

invention requirements, since they refer back to claims 1, 4 or 5.